REMARKS

Reconsideration of claims 1-3, 6-12, 40-53, 69-71 and 73-75 is respectfully requested. Claims 26-39, 54-68 and 72 are canceled by this Amendment. Claims 1, 40, 71, 74 and 75 are amended

The rejection of claims 1-3, 6-12, 40-53, 69, 70 and 73 under 35 USC 102(b) as anticipated over Yamamoto et al., JP62122671, hereafter, JP'671, is respectfully traversed. The examiner asserts that JP'671 anticipates the claims. Applicants respectfully disagree and submit a complete English translation of JP'671 for consideration, and to better evaluate the teachings and suggestions of the reference as a whole.

The JP'671 application describes a viscoelastic composition that comprises hyaluronic acid (HA), hydroxypropylmethyl cellulose (HPMC) or a mixture thereof, and a salt of carbonate or hydrogen carbonate. The JP'671 application also describes a special mixing process to maintain the homogeneity of the composition, that is, to prevent one or more components from precipitating out of the aqueous solution. The final concentration of HA, HPMC or any mixture thereof is preferably maintained from 1% to 2 w/v%. Accordingly, the most generous reading of JP'671 describes that the HPMC and HA can be used alone (independently of the other), as shown by the provided examples, or used as a mixture, and that the concentration of HA, HPMC or a mixture thereof be from 1.0 to 2.0 w/v%.

The teachings of JP'671 as a whole do not anticipate the claims for at least two reasons. First, there is no description in JP'671 of any pseudoplasticity index. The pseudoplasticity index is a measure of the difference in viscosity of the composition at or near zero shear (viscosity at 0.009 s^{-1}) to the viscosity at high shear (viscosity at 369 s^{-1}). Second, there is no description in JP'671 of having a weight ratio of HPMC to HA from 0.1 to 1.0. The examiner's rejection fails to recognize the importance of the weight ratio, and how this weight ratio is required if the composition is to possess the claimed pseudoplasticity index. There is no specific description in JP'671 of such a mixture having the claimed weight ratio, and consequently, the claimed pseudoplasticity index.

Furthermore, Applicants respectfully disagree with the examiner's statement that "Yamamoto et al. anticipates the claims *if* their composition has the same claimed pseudoplasticity index." Office Action, page 3 (bottom), *emphasis added.* That is an incorrect statement of the law.

To anticipate a claim, a single reference must contain all of the elements of the claim. Essentially, the law requires identity between the claims and the reference, though the reference need not include the identical terminology. The reference must, however, "sufficiently describe the claimed invention to have placed the public in possession of it." *Minnesota Mining & Mfg. Co. vs. Johnson & Johnson Orthopedics, Inc.*, 976 F.2d 1559 (Fed. Cir. 1992). Applicants respectfully submit that the disclosure of JP'671 does not satisfy this test for the following reasons.

The primary focus in JP'671 is to a viscoelastic composition that contains HA, HPMC or a mixture thereof with hydrogen carbonate and glucose. More importantly, there is no teaching of the necessity to even provide a mixture of HA and HPMC, let alone the claimed weight ratio, and the resulting pseudoplasticity index. Because the disclosure of JP'671 does not put the public in possession of the invention, there is no anticipation. Accordingly, Applicants respectfully request that the rejection be withdrawn.

The rejection of claims 1-3, 6-12 40-53, 69, 70 and 73 under 35 USC 103(c) as obvious over JP'671, is respectfully traversed. Applicants respectfully disagree with the examiner's statement that "Yamamoto et al. renders the claims as being obvious if their composition has a pseudoplasticity index that is substantially close to the pseudoplasticity index of Applicant's claimed composition." Office Action, pages 3-4. Again, that is an incorrect statement of the law, and improperly presupposes that there is some teaching or suggestion in JP'671 of the claimed weight ratio and resulting pseudoplasticity index. There is no such disclosure.

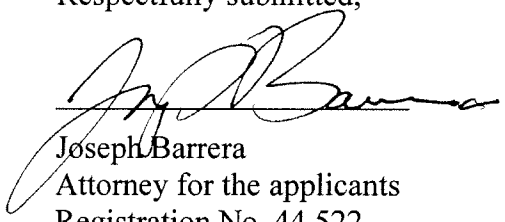
The examiner's argument must fail for the same reasons provided above. Obviousness is not a fall back position to anticipation. Rather, obviousness still requires that each and every element of the claimed invention be described or suggested in at least one reference.

The JP'671 application broadly describes a viscoelastic composition comprising HA, HPMC or a mixture thereof with a compositional range from 1.0 to 2.0 wt.%. Applicants also claim a viscoelastic composition comprising HA and HPMC, but Applicant's invention goes a few steps further. First, Applicant's invention is limited to a mixture whereas JP'671 states that HA or HPMC alone is also acceptable. Second, Applicants' invention is limited to a specific weight ratio of HA and HPMC. Because there is no such teaching or suggestion in JP'671, or because JP'671 does not put the public in possession of the Applicants' invention, Applicants respectfully request that the rejections under § 102(b) and §103(a) be withdrawn.

In view of the above, it is submitted that the claims are patentable and in condition for allowance.

May 7, 2007

Respectfully submitted,



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(12) PUBLICATION OF UNEXAMINED PATENT APPLICATION (A)
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Examination requested: not yet requested
Number of Inventions: 1 (total of 3 pages)

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(54) Title of the Invention: PRODUCTION OF HIGHLY VISCOUS LIQUID FOR INTRAOCULAR SURGERY

(21) Application Number: 60-263526
(22) Filing Date: November 23, 1985

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Clean Copy of the Specifications (No Changes of the Content)

Specifications

1. Title of the Invention: PRODUCTION OF HIGHLY VISCOUS LIQUID FOR INTRAOCULAR SURGICERY

2. Scope of the Patent's Claim

Production of highly viscous liquid for intraocular surgery, characterized by the fact that hydroxyl propyl methyl cellulose and (or) hyaluronic acid are dissolved in a buffer liquid containing saline and (or) glucose, and after an aqueous solution of an alkaline metal salt of carbonate or hydrogen carbonate has been added to this mixture, pH is adjusted to a level from 6 to 8.

3. Detailed Explanation of the Invention

(Sphere of Industrial Use)

This invention relates to a method to manufacture highly viscous liquid for intraocular surgery.

(Prior Art Technology)

Although highly viscous liquids have been widely used in intraocular surgery in order to dissolve sodium hyaluronic acid in a phosphate buffer, because such liquids are not necessarily cheap, products that would have the same effect and that would replace them are being demanded.

Moreover, highly viscous liquids containing dissolved hydroxyl propyl methyl cellulose (hereinafter abbreviated as HPMC) are used as highly viscous liquids for intraocular surgery with buffers which contain calcium ions and magnesium.

(Problem Areas to Be Solved By This Invention)

The inventors of this invention came to understand, based on their research, that highly viscous liquid which are very useful for intraocular surgery can be obtained when HPMC and (or) sodium hyaluronic acid is dissolved in a buffer containing glucose and hydrogen carbonate ions. However, they also found out when such a highly viscous liquid is prepared so that HPMC and (or) sodium hyaluronic acid are dissolved, the content amount of ions of hydrogen carbonate ions is greatly reduced, and in some cases the entire content amount is eventually dissolved, so that the concentration of hydrogen carbonate ions in the target product is insufficient.

(Means to Solve Problems)

The buffer solution which is used according to this invention is a buffer solution which can be used with a composition having a hydatoid composition prepared with various types of

salts. For example, a mixture of halogenized compounds of sodium, or a mixture containing potassium calcium and other alkaline metal or alkaline rare metals,

[page 2]

or a sulfuric acid salt, nitric acid salt or another inorganic salt, an acetic acid salt, citric acid salt, tartaric acid salt or another organic salt or another suitably mixed mixture can be used, as it is desirable to prepare a composition with a concentration and characteristics that are similar to those of a hydatoid intraocular fluid. Specifically, a desirable salt concentration is in the approximate range of 0.8 ~ 1.2 W/V%, preferably 0.9 ~ 1.1%, and desirable liquid characteristics range (fluidity) is approximately 6 ~ 8, or preferably close to neutral. As concrete examples of such salts can be named sodium chloride, potassium chloride, magnesium sulfate, or sodium citrate; wherein a buffer solution, etc., is used so as to create a total concentration of sodium chloride or the like of 1 W/V%. A desirable sugar to be used is for example glucose, xylitol, etc., and a desirable sugar concentration is in the range from 0.1 to 0.2 W/V%.

According to this invention, first, HPMC and (or) hyaluronic acid is dissolved in a buffer, such as the buffers described above. The dissolution is induced so as to create an amount creating a final product viscosity of HPMC, and so that the viscosity of the final hyaluronic acid product is in the approximate range from 1,000 to10,000 centipoise. Specifically, an addition amount can be used so as to create a concentration of approximately 0.5 to 5.0 W/V%, preferably 1.0 to 2.0 W/V%. Heating can be also applied at a suitable level when HPMC is dispersed in the buffer solution. A suitable temperature to be used during the dispersion is in the vicinity of 70 ~ 90°C and dispersing is usually conducted at 75 ~ 85°C. In order to achieve dispersing, HPMC should be added with as small additive amounts as possible while stirring is conducted on a sufficient level.

According to this invention, an aqueous solution containing hydrocarbon ions is added to an aqueous solution of dissolved HPMC. As a source of hydrocarbon ions in this aqueous solution can be used for example sodium hydrogen carbonate, potassium hydrogen carbonate or a similar alkaline metal carbonate or hydrogen carbonate can be employed. The amount of carbonate or hydrogen carbonate in an aqueous solution containing a hydrogen carbonate ions can be adjusted by inducing dissolution with a small amount of water. Any other components which are commonly used can be also utilized in the aqueous solution containing hydrogen carbonate ions, as long as this is not contrary to the objective of this invention. When an aqueous solution is added which contains hydrogen carbonate ions ahead of time to a buffer solution, a status can be created in which the temperature of the liquid of the buffer solution is not very high.

The temperature of the liquid when the aqueous solution is added should be preferably less than 20°C, or at least below room temperature. The addition should be performed as much as possible gradually, which is followed by stirring to an extent sufficient to create a homogeneous system. Next, liquid characteristics of the highly viscous liquid obtained with the addition of an aqueous solution containing hydrogen carbon ions are adjusted. The adjustment of

liquid characteristics can be performed so that the liquid is being stirred, and hydrochloride, sodium hydroxide or a similar reagent which is commonly used to adjust liquid characteristics is added to create a pH level of about 6 to 8.

The highly viscous liquid obtained in this manner has a viscosity that is suitable for intraocular surgery, that is to say a viscosity from about 1,000 to about 10,000 centipoise. Moreover, the composition should be selected so as to obtain a composition that is effective for intraocular surgery.

(Operation)

The highly viscous liquid for intraocular surgery is stored sealed at a stable temperature, which makes it possible to maintain the stability of the hydrogen carbonate ions contained in the composition, namely in an ampoule, in a vial or in a similar contained enabling long term storage so that it can be used for intraocular surgery as needed.

(Embodiments)

(Embodiment 1)

0.7 g of sodium chloride, 0.004 g of potassium chloride, 0.03 g of magnesium sulfate, 0.15 g of glucose, 0.06 g of sodium acetate, 0.1 g of sodium citrate and 0.02 g of potassium chloride were dissolved in 75 ml of sterilized pure water, this mixture was then heated to about 80°C and 2 g of HPMC were gradually added in small amounts and dissolved to a sufficient extent. After cooling, 0.2 g of sodium hydrogen carbonate were dissolved in 20 ml of sterilized pure water and added to the obtained solution as described above so that after a homogenous liquid was created, small amounts of 0.1hydrochloric acid were added to adjust the pH level to 7.4. Further, sterilized pure water was added to create a total amount of 100 ml, and after compression filtration, the mixture was injected into individual 5 ml ampoules, so that after the ampoules were filled, heating and sterilization were performed to obtain the desired product in the form of a highly viscous liquid for intraocular surgery.

(Embodiment 2)

0.7 g of sodium chloride, 0.004 g of potassium chloride, 0.03 g of magnesium sulfate, 0.15 g of glucose,

[page 3]

0.06 g of sodium acetate, 0.1 g of sodium citrate and 0.02 g of calcium chloride were dissolved in 75 ml of sterilized pure water and this mixture was stirred in dissolved in 1 g of sodium hyaluronic acid while stirring was applied at room temperature. Next, 0.2 g of sodium hydrogen

carbonate was dissolved in 20 ml of sterilized pure water, and added to the obtained liquid as described above, a homogenous liquid was created, and while stirring was applied, small amounts of 0.1 hydrochloric acid were added to adjust the pH level to 7.4. Further, sterilized pure water was added to create a total amount of 100 ml, and after compression filtration, the mixture was injected into individual 5 ml ampoules, so that after the ampoules were filled, heating and sterilization were performed to obtain the desired product in the form of a highly viscous liquid for intraocular surgery.

(Effect of the Invention)

The method of this invention makes it possible to preserve in a stable manner hydrogen carbonate ions in an highly viscous liquid used for intraocular surgery wherein HPMC and (or) hyaluronic acid is dissolved in an aqueous solution containing a salt and (or) glucose, which makes it possible to obtain a highly viscous liquid that is extremely effective for prevention of corneal disorders during intraocular surgery.

Patent Applicant: Senju Pharma K. K. Company

PROCEDURAL AMENDMENT (METHOD)

June 2, 1986

To: Commissioner of the Japanese Patent Office

1. Case Indication: Japanese Patent Application Number 60-263526

2. Title of the Invention: Production of Highly Viscous Liquid for Intraocular Surgery

3. Amending Party

Relationship to the Case: Patent Applicant

Name: Senju Pharma K. K. Company
Osaka-shi, Higashi-ku
Yacho 3-chome, 6-banchi-1

Representative: [illegible name] [two seals]

4. Date of the Amendment Order: Voluntary

5. Subject of the Amendment: Specifications

A clean copy of the Specifications has been added to the initial application.

7. List of Attached Documents

(1) Specifications (No Change of the Content) 1 copy

PROCEDURAL AMENDMENT (VOLUNTARY)

To: Commissioner of the Japanese Patent Office

1. Case Indication: Japanese Patent Application Number 60-263526

2. Title of the Invention: Production of Highly Viscous Liquid for Intraocular Surgery

3. Amending Party

Relationship to the Case: Patent Applicant

Name: Senju Pharma K. K. Company
Osaka-shi, Higashi-ku
Yacho 3-chome, 6-banchi-1

4. Date of the Amendment Order: Voluntary

5. Number of Inventions Added by the Amendment: 0

6. Subject of the Amendment: Colum "Detailed Explanation of the invention" in the Specifications

7. Content of the Amendment

(1) The text from line 6 ~ 6 on page 3 of the Specifications is changed from "about 0.9 ~ 1.1%, the fluidity is about 6 ~ 8" to "about 0.9 ~ 1.1 W/V%", the pH level is about 6 ~ 8".

(2) The text in line 6 on page 5 of the Specifications is changed from "conducted" to "is carried out".

THAT IS ALL

Date Stamp: March 28, 1986